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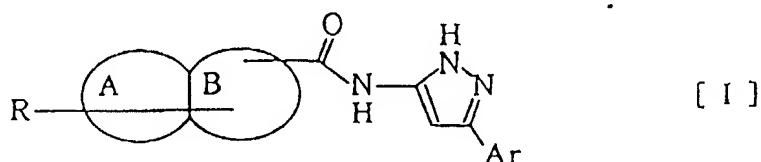
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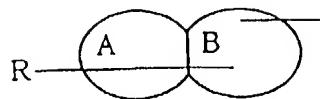
(57) The present invention relates to a compound represented by the general formula [I]:



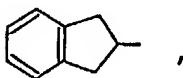
wherein A and B rings are ortho-condensed to each other, A ring represents an aromatic carbocyclic or heterocyclic ring and B ring represents an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed; Ar represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; and R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, provided that when the group represented by

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is the group represented by



Ar is not a phenyl group nor a 4-chlorophenyl group,
or its salt, a method for its preparation as well as an agent for the treatment of bulimia, obesity or diabetes comprising
it as an active ingredient.

Description**FIELD OF THE INVENTION**

- 5 [0001] The present invention is useful in the field of medicines. More specifically, novel pyrazole derivatives of the present invention are useful as neuropeptide Y receptor antagonists and as agents for the treatment of various diseases of circulatory organs, central nervous system and metabolic system.

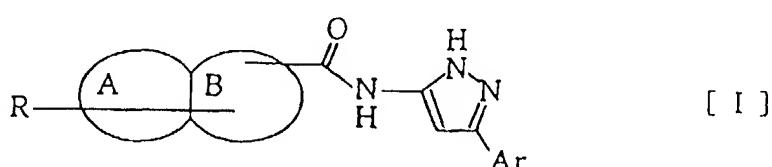
BACKGROUND OF THE INVENTION

- 10 [0002] Neuropeptide Y (to be referred to as NPY hereinafter) is a peptide consisting of 36 amino acids, which was isolated from porcine brain for the first time by Tatsumoto et al. in 1982 [Nature, vol.296, p.659 (1982)]. NPY is broadly distributed in central and peripheral nervous systems and has various *in vivo* functions as one of the peptides most abundantly present in the nervous system. That is, in the central nervous system, NPY acts as an aperitive and significantly promotes a fat accumulation via secretion of various hormones and actions of the nervous system. It is known that a continuous intracerebroventricular administration of NPY induces obesity and insulin resistance based on the above actions. NPY is also associated with the control of mood and functions of the central autonomic nervous system. In addition, in the peripheral nervous system, NPY is present together with norepinephrine in the sympathetic nerve terminal and associated with the tension of the sympathetic nervous system. It is known that a peripheral administration 20 of NPY causes vasoconstriction and enhances actions of other vasoconstrictors including norepinephrine [International Journal of Obesity, vol.19, p.517 (1995); Endocrinology, vol.133, p.1753 (1993); British Journal of Pharmacology, vol.95, p.419 (1988)].
- [0003] The function of NPY is expressed when it is bound to an NPY receptor present in the central or peripheral nervous system. Therefore, the expression of the function of NPY can be prevented if the binding of NPY to the NPY receptor is inhibited. Consequently, it is expected that compounds capable of inhibiting the binding of NPY to the NPY receptor are useful in the prevention or treatment of various diseases associated with NPY, for example, diseases of circulatory organs such as hypertension, nephropathy, cardiopathy and angiospasm; diseases of central nervous system such as bulimia, depression, epilepsy and dementia; metabolic diseases such as obesity, diabetes and dysendocrinosis; or glaucoma [Trends in Pharmacological Sciences, vol.15, p.153 (1994)].
- 30 [0004] Compounds structurally similar to the compounds of the present invention are disclosed in International Publication WO 96/14843, JP 3093774A, JP 2300173A, JP 51146465A and etc. However, these publications do not clearly disclose nor suggest the compound of the present invention. And, an antagonistic action to NPY is not described at all therein.

DISCLOSURE OF THE INVENTION

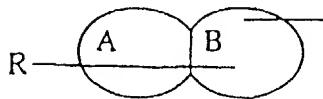
[0005] An object of the present invention is to provide a new medicine having an antagonistic action to NPY.

[0006] The present inventors found that a compound represented by the general formula [I]:



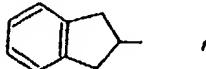
- wherein A and B rings are ortho-condensed to each other, A ring represents an aromatic carbocyclic or heterocyclic ring and B ring represents an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed; Ar represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; and R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, provided that when the group represented by

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is the group represented by

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- 15 Ar is not a phenyl group nor a 4-chlorophenyl group.
has an antagonistic action to NPY.

[0007] Since the compound [I] of the present invention has the antagonistic action to NPY, it is useful as an agent for the treatment of various diseases associated with NPY, for example, diseases of circulatory organs such as hypertension, nephropathy, cardiopathy and angiospasm, diseases of central nervous system such as bulimia, depression, epilepsy and dementia, metabolic diseases such as obesity, diabetes and dysendocrinosis, or glaucoma.

[0008] Especially, the compound [I] of the present invention is useful as an agent for the treatment of bulimia, obesity, diabetes or the like.

[0009] The present invention relates to a compound represented by the general formula [I] or its salt as well as a method for its preparation and its use.

- 25 [0010] Symbols and terms as used herein are described below.

[0011] The term "aromatic carbocyclic ring" as used herein means benzene, naphthalene or anthracene ring.

[0012] The term "aromatic heterocyclic ring" as used herein means a 5- or 6-membered monocyclic aromatic heterocyclic ring containing 1 or more, preferably 1 to 3, of heteroatoms which may be the same or different and are selected from the group consisting of oxygen, nitrogen and sulfur, or a condensed aromatic heterocyclic ring in which said monocyclic aromatic heterocyclic ring and the aforementioned aromatic carbocyclic ring are condensed or in which the same or different members of said monocyclic aromatic heterocyclic rings are mutually condensed, and its illustrative examples include pyrrole, furan, thiophene, imidazole, pyrazole, thiazole, isothiazole, oxazole, isoxazole, triazole, oxadiazole, thiadiazole, pyridine, pyrazine, pyrimidine, pyridazine, indole, benzofuran, benzothiophene, benzimidazole, benzoxazole, benzisoxazole, benzothiazole, benzisothiazole, indazole, purine, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline and pteridine rings and the like.

[0013] The term "aliphatic carbocyclic ring" as used herein means a carbocyclic ring whose ring atoms other than those involved in the condensation are mutually bound as saturated bonds, and its illustrative examples include cyclobutane, cyclobutene, cyclopentane, cyclopentene, cyclohexane, cyclohexene, cycloheptane and cycloheptene rings and the like.

40 [0014] The term "aliphatic nitrogen-containing heterocyclic ring" as used herein means a nitrogen-containing heterocyclic ring which contains one nitrogen atom and whose ring atoms other than those involved in the condensation are mutually bound as saturated bonds, and its illustrative examples include azetidine, pyrrolidine, piperidine and perhydroazepine rings and the like.

[0015] The term "halogen atom" as used herein means fluorine, chlorine, bromine or iodine.

45 [0016] The term "lower alkyl group" as used herein means a straight, branched or cyclic alkyl group containing 1 to 7 carbon atoms, and its illustrative examples include methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, neopentyl, tert-pentyl, 1-methylbutyl, 2-methylbutyl, 1,2-dimethylpropyl, 1-ethylpropyl, hexyl, isohexyl, 1-methylpentyl, 2-methylpentyl, 3-methylpentyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 2,2-dimethylbutyl, 1-ethylbutyl, 1,1,2-trimethylpropyl, 1,2,2-trimethylpropyl, 1-ethyl-2-methylpropyl, 1-ethyl-1-methylpropyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclopropylmethyl, 1-cyclopropylethyl, 2-cyclopropylethyl, 1-cyclopropylpropyl, 2-cyclopropylpropyl, 3-cyclopropylpropyl, cyclopentylmethyl, 2-cyclopentylethyl and cyclohexylmethyl and the like.

[0017] The term "lower alkenyl group" as used herein means a straight or branched alkenyl group containing 2 to 7 carbon atoms, and its illustrative examples include vinyl, 2-propenyl, isoproponyl, 3-butenyl, 2-butenyl, 1-butenyl, 1-methyl-2-propenyl, 1-methyl-1-propenyl, 1-ethyl-1-ethenyl, 2-methyl-2-propenyl, 2-methyl-1-propenyl, 3-methyl-2-butenyl and 4-pentenyl and the like.

55 [0018] The term "lower haloalkyl group" as used herein means the above lower alkyl group comprising the aforementioned halogen atom, and its illustrative examples include fluoromethyl, difluoromethyl, trifluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, chloromethyl, dichloromethyl, trichloromethyl, 1-chloroethyl and 2-

chloroethyl and the like.

[0019] The term "lower alkoxy group" as used herein means an alkoxy group comprising the aforementioned lower alkyl group, namely an alkoxy group containing 1 to 7 carbon atoms, or an alkyleneoxy group containing 1 to 3 carbon atoms, and its illustrative examples include methoxy, ethoxy, propyloxy, isopropylmethoxy, butoxy, isobutoxy, tert-butoxy, pentyloxy, cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy, cycloheptyloxy, cyclopropyl-methoxy, 1-cyclopropylethoxy, 2-cyclopropylethoxy, 1-cyclopropylpropyloxy, 2-cyclopropylpropyloxy, 3-cyclopropyl-propyloxy, cyclopentylmethoxy, 2-cyclopentylethoxy, cyclohexylmethoxy, methylenedioxy, ethylenedioxy and trimethylenedioxy and the like.

[0020] The term "lower alkylthio group" as used herein means an alkylthio group comprising the aforementioned lower alkyl group, namely an alkylthio group containing 1 to 7 carbon atoms, and its illustrative examples include methylthio, ethylthio, propylthio, isopropylthio, butylthio, isobutylthio, tert-butylthio, pentythio, cyclopropylthio, cyclobutylthio; cyclopentylthio, cyclohexylthio, cycloheptylthio, cyclopropylmethylthio, 1-cyclopropylethylthio, 2-cyclopropylethylthio, 1-cyclopropylpropylthio, 2-cyclopropylpropylthio, 3-cyclopropylpropylthio, cyclopentylmethylthio, 2-cyclopentylethylthio and cyclohexylmethylthio and the like.

[0021] The term "lower alkylamino group" as used herein means an amino group monosubstituted with the aforementioned lower alkyl group, and its illustrative examples include methylamino, ethylamino, propylamino, isopropylamino, butylamino, sec-butylamino and tert-butylamino and the like.

[0022] The term "lower dialkylamino group" as used herein means an amino group disubstituted with the aforementioned lower alkyl group, and its illustrative examples include dimethylamino, diethylamino, ethylmethylamino, dipropylamino, methylpropylamino and diisopropylamino and the like.

[0023] The term "aromatic carbocyclic ring group" as used herein means a group derived from the aforementioned aromatic carbocyclic ring, and its illustrative example include phenyl, naphthyl or anthryl.

[0024] The term "aromatic heterocyclic ring group" as used herein means a group derived from the aforementioned aromatic heterocyclic ring, and its illustrative example include pyrrolyl, furyl, thieryl, imidazolyl, pyrazolyl, thiazolyl, iso-thiazolyl, oxazolyl, isoxazolyl, triazolyl, oxadiazolyl, thiadiazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, indazolyl, purinyl, quinolyl, isoquinolyl, phthalazinyl, naphthyridinyl, quinoxalinyl, quinazolinyl, cinnolinyl and pteridinyl and the like.

[0025] The "salt" of the compound represented by the general formula [I] means any conventional pharmaceutically acceptable salt, and its examples include acid addition salts based on basic groups such as a basic heterocyclic ring group or an amino substituent and the like.

[0026] Illustrative examples of the acid addition salt include an inorganic salt such as hydrochloride, sulfate, nitrate, phosphate and perchlorate; an organic salt such as maleate, fumarate, tartarate, citrate, ascorbate and trifluoroacetate; and sulfonate such as methanesulfonate, isethionate, benzenesulfonate and p-toluenesulfonate.

[0027] The term "agent for the treatment" as used herein means a drug to be used for the treatment and/or prevention of various diseases.

[0028] Various symbols used in the general formula [I] are described further in detail with reference to its preferred embodiment in order to explain the compound represented by the general formula [I] of the present invention more clearly.

[0029] A and B rings are ortho-condensed to each other and A ring means an aromatic carbocyclic or heterocyclic ring and B ring means an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed.

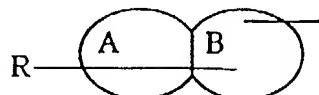
[0030] Preferred examples of the aromatic carbocyclic ring as A ring include benzene and naphthalene rings and those of the aromatic heterocyclic ring as A ring include indole, benzofuran, benzothiophene and quinoline rings.

[0031] Preferred examples of the aliphatic four- to seven-membered carbocyclic ring as B ring include cyclopentane, cyclopentene, cyclohexane and cyclohexene rings.

[0032] Preferred examples of the aliphatic four- to seven-membered nitrogen-containing carbocyclic ring as B ring include pyrrolidine ring.

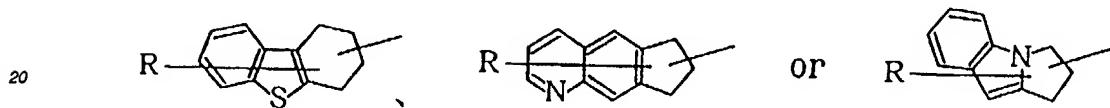
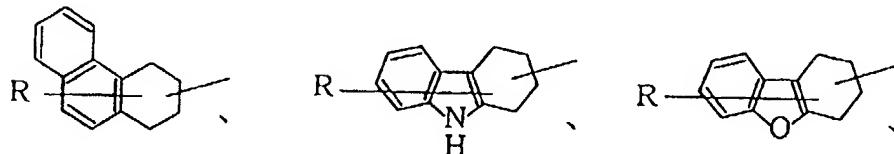
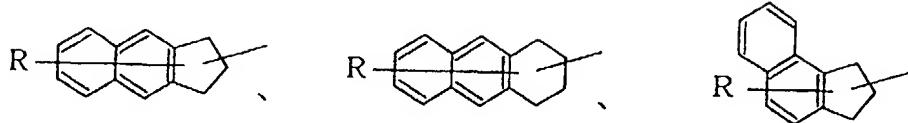
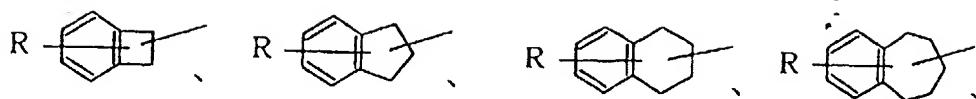
[0033] In consequence, preferred examples of the group represented by the formula:

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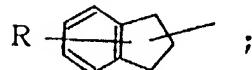


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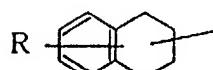
wherein R is a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, includes



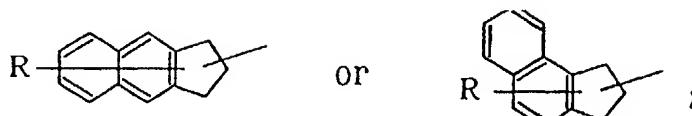
25 wherein R is as defined above, of which
the group represented by the formula:



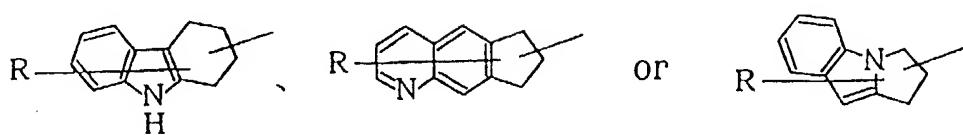
the group represented by the formula:



40 the group represented by the formula:



or the group represented by the formula:

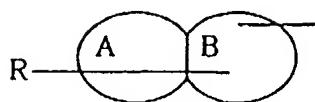


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is preferred.

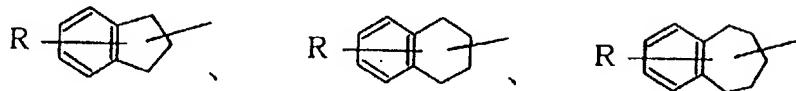
[0034] Though the compounds wherein the group represented by the formula:

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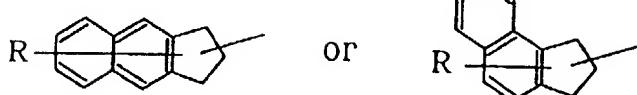


is the group represented by the formula:

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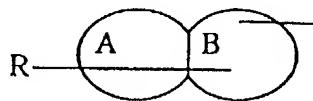


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- 20 wherein R is as defined above, are included in the scope of the invention, the groups exemplified above are preferred.
 [0035] With respect to the bond between the group represented by the formula:

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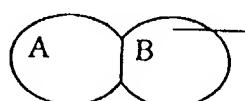


- 30 and the adjacent carbonyl group, the carbon atom of the carbonyl group is preferably bound to B ring on any ring atom thereof other than those involved in the condensation with A ring.

[0036] R means a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

- 35 [0037] As the substituent, 1 or more, preferably 1 or 2, substituents which may be the same or different can be selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group. Said substituent can be present at any substitutable position on the group represented by the formula:

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- 45 wherein A and B rings are as defined above.

[0038] Preferred examples of the halogen atom as said substituent include chlorine and bromine.

[0039] Preferred examples of the lower alkyl group as said substituent include methyl and ethyl.

[0040] Preferred examples of the lower alkoxy group as said substituent include methoxy, ethoxy, propyloxy, isopropoxy and methylenedioxy, of which methoxy and methylenedioxy are more preferable.

50 [0041] Preferred examples of the aromatic carbocyclic ring group as said substituent include phenyl.

[0042] Preferred examples of the carbonyl group having the aromatic carbocyclic ring group as said substituent include benzoyl.

[0043] As R, a hydrogen atom and a substituent such as a halogen atom and a lower alkyl group are preferred.

55 [0044] Ar means an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups.

[0045] The term "an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower

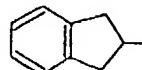
alkylamino, lower dialkylamino and aromatic carbocyclic ring groups" means the aforementioned aromatic carbocyclic or heterocyclic ring group unsubstituted or substituted at any substitutable position with 1 or more, preferably 1 or 2, substituents which may be the same or different and are selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups.

- 5 [0046] Preferred examples of the halogen atom as said substituent include chlorine and bromine.
- [0047] Preferred examples of the lower alkyl group as said substituent include methyl, ethyl, propyl and butyl.
- [0048] Preferred examples of the lower alkenyl group as said substituent include vinyl, 2-propenyl, isopropenyl, 2-but enyl and 3-methyl-2-but enyl, of which vinyl and 2-propenyl are more preferred.
- 10 [0049] Preferred examples of the lower haloalkyl group as said substituent include fluoromethyl and trifluoromethyl.
- [0050] Preferred examples of the lower alkoxy group as said substituent include methoxy, ethoxy, propyloxy, isopro poxy and methylenedioxy, of which methoxy and methylenedioxy are more preferred.
- [0051] Preferred examples of the lower alkylthio group as said substituent include methylthio, ethylthio and propylthio, of which methylthio is more preferred.
- 15 [0052] Preferred examples of the lower alkylamino group as said substituent include methylamino.
- [0053] Preferred examples of the lower dialkylamino group as said substituent include dimethylamino.
- [0054] Preferred examples of the aromatic carbocyclic ring group as said substituent include phenyl.
- [0055] As said substituent, a halogen atom and a lower alkyl, lower alkoxy, lower alkylthio or lower dialkylamino group are more preferred.
- 20 [0056] Preferred examples of the aromatic carbocyclic ring group as Ar include phenyl and naphthyl, and those of the aromatic heterocyclic ring group include pyridyl.
- [0057] In consequence, preferred examples of Ar include phenyl, 1-naphthyl, 2-naphthyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 5-chloro-3-pyridyl, 5-bromo-3-pyridyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 3-ethylphenyl, 4-ethylphenyl, 4-propylphenyl, 5-methyl-2-pyridyl, 6-methyl-3-pyridyl, 6-ethyl-3-pyridyl, 2-methyl-4-pyridyl, 2-ethyl-4-pyridyl, 2-propyl-4-pyridyl, 2-butyl-4-pyridyl, 3-methyl-4-pyridyl, 3-vinylphenyl, 4-vinylphenyl, 4-(2-propenyl)phenyl, 5-vinyl-3-pyridyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 4-isopropoxyphenyl, 3,4-dimethoxyphenyl, 3,4-methylenedioxypyhenyl, 6-methoxy-3-pyridyl, 2-methoxy-4-pyridyl, 3-dimethylaminophenyl, 4-dimethylaminophenyl, 4-methoxy-3-dimethylaminophenyl, 2-methylthiophenyl, 3-methylthiophenyl, 4-methylthiophenyl, 2-methylthio-4-pyridyl, 3-biphenyl and 4-biphenyl, of which 4-pyridyl, 2-methyl-4-pyridyl, 2-ethyl-4-pyridyl, 2-propyl-4-pyridyl, 2-butyl-4-pyridyl, 3-chlorophenyl, 4-chlorophenyl, 3,4-dichlorophenyl, 3-bromophenyl, 4-bromophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 4-ethylphenyl, 3-methyl-4-pyridyl, 3-ethyl-4-pyridyl, 4-vinylphenyl, 4-(2-propenyl)phenyl, 3-methoxyphenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 3,4-dimethoxyphenyl, 3,4-methylenedioxypyhenyl, 3-methoxy-4-pyridyl, 4-methylthiophenyl and 3-methylthio-4-pyridyl are more preferred.
- 35 [0058] A compound wherein the group represented by the formula:



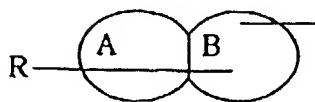
45 is a group represented by the formula:

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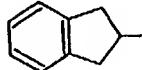
and Ar is a phenyl group and a compound wherein the group represented by the formula:

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is a group represented by the formula:

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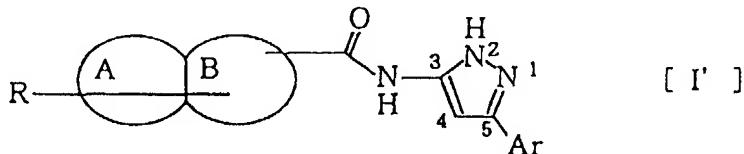
15 and Ar is 4-chlorophenyl are excluded from the scope of the present invention.

[0059] Depending on the nature of substituent, the compounds of the present invention may exists in various stereoisomers including optical isomers, diasteromers and geometrical isomers, and tautomers. All of these stereoisomers and tautomers and their mixtures are also included in the present invention.

[0060] In this connection, in order to avoid unnecessary confusion in naming each of the compounds of the present

20 invention, position numbers of the pyrazole ring moiety of the compound represented by the general formula [I] are defined as shown in the following general formula [I'], and the nomenclature and other explanations of each compound are described based on this formula.

25



30

[0061] Illustrative examples of the compound represented by the general formula [I] include:

- 35 3-(2-indanyl)carbonylamino-5-(4-methylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(3-methylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(2-methylphenyl)pyrazole,
 5-(4-chlorophenyl)-3-(1-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(3-methoxyphenyl)pyrazole,
 40 5-(3-chlorophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3,4-dichlorophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(2-pyridyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(4-pyridyl)pyrazole,
 45 3-(2-indanyl)carbonylamino-5-(2-methoxyphenyl)pyrazole,
 5-(4-chlorophenyl)-3-(1,2,3,4-tetrahydro-1-naphthyl)carbonylaminopyrazole,
 5-(2-chlorophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(3-pyridyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(1-naphthyl)pyrazole,
 50 3-(2-indanyl)carbonylamino-5-(2-naphthyl)pyrazole,
 5-(4-dimethylaminophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-dimethylaminophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-isopropoxyphenyl)pyrazole,
 55 5-(4-ethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-trifluoromethylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(3-trifluoromethylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(4-methylthiophenyl)pyrazole,

3-(2-indanyl)carbonylamino-5-(3,4-methylenedioxyphenyl)pyrazole,
 5-(3-dimethylamino-4-methoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydro-2-naphthyl)carbonylaminopyrazole,
 5-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 5-(4-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-vinylphenyl)pyrazole,
 10 3-(2-indanyl)carbonylamino-5-(3-vinylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(4-(2-propenyl)phenyl)pyrazole,
 5-(4-biphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-biphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 15 5-(4-ethylphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-ethylphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-propylphenyl)pyrazole,
 5-(4-methoxyphenyl)-3-(2-methyl-2-indanyl)carbonylaminopyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 (+)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 20 (-)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 3-(5,6-dichloroindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(5-chloroindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(5,6-dichloroindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 25 3-(4-bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 3-(5-bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 5-(4-methoxyphenyl)-3-(4-phenylindan-2-yl)carbonylaminopyrazole,
 3-(4-phenylindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 30 (+)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 (-)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-methylpyridin-4-yl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-propylpyridin-4-yl)pyrazole,
 35 5-(2-butylpyridin-4-yl)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylaminopyrazole,
 3-(bicyclo[4.2.0]oct-1(6),2,4-trien-7-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 5-(4-methoxyphenyl)-3-(5-nitroindan-2-yl)carbonylaminopyrazole,
 5-(4-methoxyphenyl)-3-(4-nitroindan-2-yl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrocarbazol-2-yl)carbonylaminopyrazole,
 3-(5-benzoylindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 40 3-(5-benzoylindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrodibenzo[b,d]furan-3-yl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(9-methyl-1,2,3,4-tetrahydrocarbazol-2-yl)carbonylaminopyrazole,
 3-(2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]indol-2-yl)-5-(4-methoxyphenyl)carbonylaminopyrazole,
 45 3-(7,8-dihydro-6H-cyclopenta[g]quinolin-7-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 5-(2-ethylpyridin-4-yl)-3-(2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrodibenzo[b,d]thiophen-3-yl)carbonylaminopyrazole,
 5-(4-methoxyphenyl)-3-(4-methyl-2,3-dihydro-1H-cyclopenta[b]indol-2-yl)carbonylaminopyrazole, and
 5-(4-methoxyphenyl)-3-(5-phenylindan-2-yl)carbonylaminopyrazole.

50 [0062] Next, processes for the preparation of the compound of the present invention are described below.

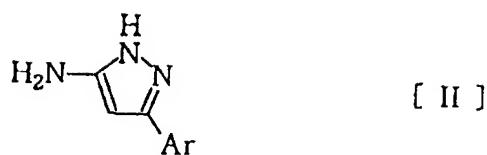
[0063] The compound represented by the general formula [I] can be prepared, for example, by one of the following processes or the methods as shown in examples, provided that the process for the preparation of the compound [I] of the present invention is not limited thereto.

55

Process 1

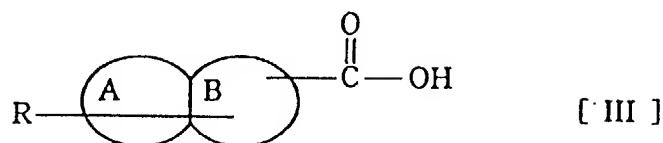
[0064] The compound represented by the general formula [I] can be prepared by reacting a compound represented

by the general formula [II]:



10 wherein Ar is as defined above,

with a carboxylic acid represented by the general formula [III]:



20

wherein A and B rings and R are as defined above,
or its reactive derivative.

[0065] The reaction of the compound of the general formula [II] with the carboxylic acid of the general formula [III] is generally carried out using 0.5 mole to excess moles, preferably 1 mole to 1.5 moles, of the carboxylic acid of the general formula [III] with respect to 1 mole of the compound of the general formula [II].

[0066] The reaction is generally carried out in an inert solvent, and preferred examples of said inert solvent include methylene chloride, chloroform, tetrahydrofuran, dimethylformamide and pyridine and a mixture thereof.

[0067] Also, it is desirable to carry out the reaction in the presence of a condensing agent, and examples of said condensing agent to be used include N,N'-dicyclohexylcarbodiimide, N,N'-diisopropylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluorophosphate, benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate, bromotris-(dimethylamino)phosphonium hexafluorophosphate, diphenylphosphoric acid aside and 1,1'-carbonylidimidazole.

[0068] Said condensing agent can be generally used in an amount of from 1 mole to excess moles, preferably from 1 mole to 1.5 moles, with respect to 1 mole of the compound of the general formula [II].

[0069] The reaction temperature is generally within the range of from -50°C to 100°C, preferably from -20°C to 50°C.

[0070] The reaction time is generally within the range of from 30 minutes to 7 days, preferably from 1 hour to 24 hours.

[0071] The compound of the general formula [I] can also be prepared by reacting a reactive derivative of the carboxylic acid represented by the general formula [III], in stead of said carboxylic acid, with the compound of the general formula [II].

[0072] As the reactive derivative of the carboxylic acid represented by the general formula [III], an acid halide, a mixed acid anhydride, an active ester, an active amide or the like may be used.

[0073] An acid halide of the carboxylic acid of the general formula [III] can be obtained by reacting the carboxylic acid of the general formula [III] with a halogenation agent according to any conventional method. Examples of the halogenation agent to be used include thionyl chloride, phosphorus trichloride, phosphorus pentachloride, phosphorus oxychloride, phosphorus tribromide, oxalyl chloride and phosgene.

[0074] A mixed acid anhydride of the carboxylic acid of the general formula [III] can be obtained by reacting the carboxylic acid of the general formula [III] with an alkyl chlorocarbonate such as ethyl chlorocarbonate or an aliphatic carboxylic acid chloride such as pivaloyl chloride according to any conventional method.

[0075] An active ester of the carboxylic acid of the general formula [III] can be obtained by reacting the carboxylic acid of the general formula [III] with an N-hydroxy compound such as N-hydroxysuccinimide, N-hydroxyphthalimide or 1-hydroxybenzotriazole or a phenol compound such as 4-nitrophenol, 2,4-dinitrophenol, 2,4,5-trichlorophenol or pentachlorophenol, in the presence of a condensing agent such as N,N'-dicyclohexylcarbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide according to any conventional method.

[0076] An active amide of the carboxylic acid of the general formula [III] can be obtained by reacting the carboxylic acid of the general formula [III] with 1,1'-carbonyldimidazole or 1,1'-carbonylbis(2-methylimidazole) according to any conventional method.

[0077] The reaction of the compound of the general formula [II] with the reactive derivative of the carboxylic acid of the general formula [III] is generally carried out using 0.5 mole to excess moles, preferably 1 mole to 1.5 moles, of the reactive derivative of the carboxylic acid of the general formula [III] with respect to 1 mole of the compound of the general formula [II].

5 [0078] The reaction is generally carried out in an inert solvent, and preferred examples of said inert solvent include methylene chloride, chloroform, tetrahydrofuran, dimethylformamide and pyridine and a mixture thereof.

[0079] Though the aforementioned reaction proceeds in the absence of a base, it is desirable to proceed the reaction in the presence of any base in order to proceed the reaction more smoothly.

10 [0080] Examples of said base to be used include an organic base such as triethylamine, diisopropylethylamine, pyridine or 4-dimethylaminopyridine, or an inorganic base such as sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate or sodium bicarbonate.

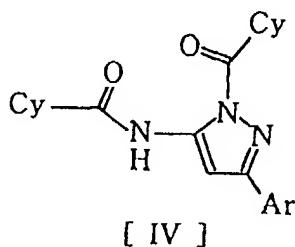
[0081] It is desirable to use said base generally in an amount of from 1 mole to excess moles with respect to 1 mole of the compound of the general formula [II]. When said base is liquid, it can be used as both a solvent and a base.

15 [0082] The reaction temperature is generally within the range of from -50°C to 100°C, preferably from -20°C to 50°C.

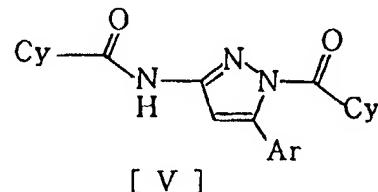
[0083] The reaction time is generally within the range of from 5 minutes to 7 days, preferably from 30 minutes to 24 hours.

[0084] In the reaction of the compound of the general formula [II] with the carboxylic acid of the general formula [III] or its reactive derivative, a compound represented by the general formula [IV] or [V]:

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wherein -Cy represents a group represented by the formula:

35



in which A and B rings and R are as defined above, and Ar is as defined above,

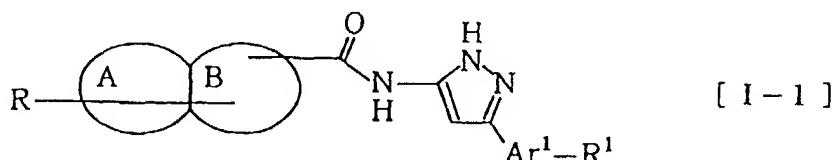
40 may be obtained as a by-product depending on the reaction conditions. Each of these compounds can be converted into the compound of the general formula [I] by hydrolyzing it in the presence of sodium hydroxide or potassium hydroxide or the like.

Process 2

45

[0085] A compound represented by the general formula [I-1]:

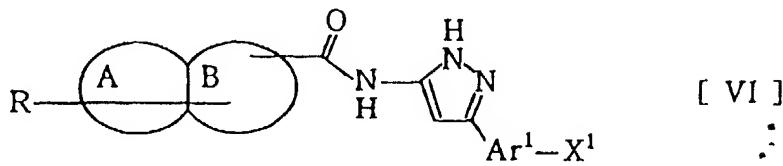
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55 wherein Ar¹ represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; R¹ represents a lower alkyl, lower alkenyl or aromatic carbocyclic

ring group; and A and B rings and R are as defined above,
can be prepared by reacting a compound represented by the general formula [VI]:

5



10

wherein X¹ represents a halogen or a trifluoromethanesulfonyloxy group; and A and B rings, Ar¹ and R are as defined above,

15 with a compound represented by the general formula [VII]:

20



wherein R^a represents a lower alkyl group and R¹ is as defined above, in the presence of a palladium catalyst.

25 [0086] The reaction of the compound of the general formula [VI] with the compound of the general formula [VII] is generally carried out using 0.5 mole to 10 moles, preferably 1 mole to 3 moles, of the compound of the general formula [VII] with respect to 1 mole of the compound of the general formula [VI].

[0087] The reaction is generally carried out in an inert solvent, and preferred examples of said inert solvent include benzene, toluene, tetrahydrofuran, dimethylformamide and N-methylpyrrolidone and a mixture thereof.

30 [0088] Examples of the palladium catalyst to be used include tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium chloride, palladium acetate and tris(benzylideneacetone)dipalladium.

[0089] Said palladium catalyst is generally used in an amount of from 0.001 mole to 1 mole, preferably from 0.01 mole to 0.1 mole, with respect to 1 mole of the compound of the general formula [VI].

35 [0090] In addition, it is possible to add a phosphine ligand such as triphenylphosphine or tri-2-furylphosphine, or lithium chloride to the reaction system in order to proceed the reaction more smoothly.

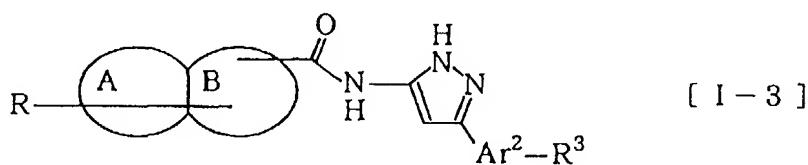
[0091] The reaction temperature is generally within the range of from room temperature to 200°C, preferably from 60°C to 150°C.

[0092] The reaction time is generally within the range of from 30 minutes to 7 days, preferably from 1 hour to 24 hours.

40 Process 3

[0093] A compound represented by the general formula [I-3]:

45

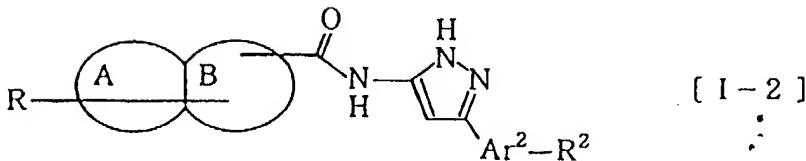


50

wherein Ar² represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; R³ represents a lower alkyl group; and A and B rings and R are as defined above,

55 can be prepared by catalytically hydrogenating a compound represented by the general formula [I-2]:

5



10 wherein R^2 is a lower alkenyl group; and A and B rings, Ar^2 and R are as defined above, in the presence of a catalyst.

[0094] The reaction is generally carried out in an inert solvent, and preferred examples of said inert solvent include methanol, ethanol, methylene chloride, chloroform, tetrahydrofuran, dimethylformamide and acetic acid and a mixture thereof.

[0095] As the catalyst to be used in the reaction, a palladium-carbon catalyst or the like is preferred.

15 [0096] The reaction temperature is generally room temperature.

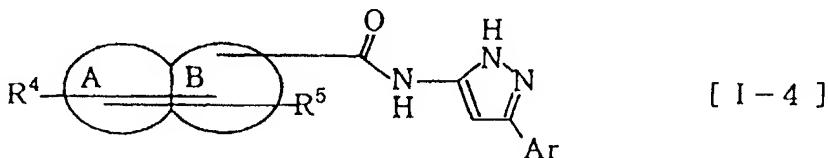
[0097] The hydrogen pressure is generally from 1 to 50 atmospheric pressure, preferably from 1 to 5 atmospheric pressure.

[0098] The reaction time is generally within the range of from 30 minutes to 7 days, preferably from 1 hour to 24 hours.

20 Process 4

[0099] A compound represented by the general formula [I-4]:

25

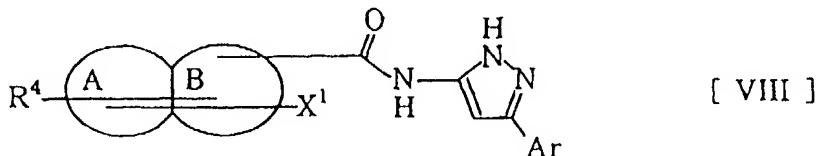


30

wherein R^4 represents a substituent selected from the group consisting of nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom; R^5 represents a lower alkyl or aromatic carbocyclic ring group; and A and B rings and Ar are as defined above.

35 can be prepared by reacting a compound represented by the general formula [VIII]:

40



45 wherein A and B rings, Ar, X^1 and R^4 are as defined above, with a compound represented by the general formula [IX]:

50



55 wherein R^5 and R^a are as defined above, in the presence of a palladium catalyst.

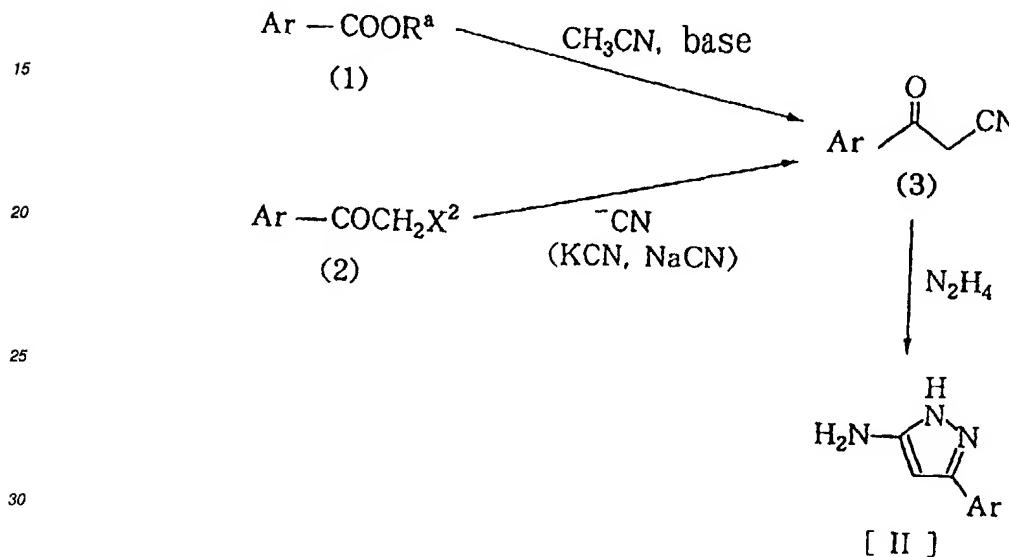
[0100] The reaction of the compound of the general formula [VIII] with the compound of the general formula [IX] is carried out in the same manner as the reaction of the compound of the general formula [VI] with the compound of the

general formula [VII] in the aforementioned Process 2. Thus, the same reaction conditions as those in Process 2 can be applied.

[0101] The compound of the general formula [I], [I-1], [I-3] or [I-4] can be easily isolated and purified by any conventional separation methods. Examples of such methods include solvent extraction, recrystallization, column chromatography and preparative thin layer chromatography.

[0102] These compounds can be converted into three pharmaceutically acceptable salts according to any conventional method and vice versa.

[0103] The compound of the general formula [II] to be used in the present invention is commercially available, or it can be prepared, for example, in accordance with the methods described in references, such as Comprehensive Heterocyclic Chemistry, vol.5, edited by A.R. Katritzky, Pergamon Press (1984) or their modifications, or alternatively with the following process or the method as described in the reference examples.



35 wherein X² represents a halogen atom; and Ar and R^a are as defined above.

[0104] According to this process, the compound of the general formula [II] can be prepared by reacting a compound represented by the general formula (1) with acetonitrile in the presence of a base to obtain a compound represented by the general formula (3), and subsequently reacting said compound (3) with hydrazine.

[0105] Conditions for the reaction of the compound (1) with acetonitrile vary depending on the nature of the base to be used.

[0106] For example, when n-butyllithium, lithium diisopropylamide or the like is used as said base, the reaction is generally carried out in an inert solvent such as tetrahydrofuran or ethyl ether at a temperature of from -78°C to room temperature for a reaction period of from 30 minutes to 6 hours.

[0107] When sodium hydride or the like is used as said base, the reaction is generally carried out in an inert solvent such as tetrahydrofuran, ethyl ether or dimethylformamide at a temperature of from room temperature to 100°C for a reaction period of from 1 hour to 6 hours.

[0108] The reaction of the compound (3) with hydrazine is generally carried out in an inert solvent such as ethanol, propanol, isoamyl alcohol, acetic acid, benzene, toluene or xylene or a mixture thereof, using hydrazine in an amount of from 0.5 mole to 10 moles, preferably from 1 mole to 1.5 moles, with respect to 1 mole of the compound (3).

[0109] The reaction temperature is generally from room temperature to the boiling point of the solvent used, preferably from 50°C to the boiling point of the solvent used.

[0110] The reaction time is generally from 30 minutes to 7 days, preferably from 1 hour to 48 hours.

[0111] The hydrazine to be used in the reaction may be either anhydride or hydrate.

[0112] In addition, the compound of the general formula (3) can also be prepared by using a compound represented by the general formula (2) in stead of the compound represented by the general formula (1), and reacting it with a cyanide.

[0113] In this connection, the compound represented by the general formula (1) or (2) is commercially available or it can be prepared in accordance with known methods or their modifications which may be suitably combined if neces-

sary.

[0114] The carboxylic acid represented by the general formula [III] to be used in the present invention is commercially available or it can be prepared according to known methods or their modifications or alternatively the method as described in the reference examples which may be suitably combined if necessary.

5 [0115] The compound represented by the general formula [VI] to be used in the present invention can be prepared using a material corresponding to the desired compound according to aforementioned process for the preparation of the compound of the general formula [II], modifications of the aforementioned Process 1 and known methods which may be suitably combined if necessary.

10 [0116] The compound represented by the general formula [VII] to be used in the present invention is commercially available or it can be prepared according to known methods or their modifications which may be suitably combined if necessary.

15 [0117] The usefulness of the compound of the present invention as a medicine is demonstrated by showing its antagonistic activity to NPY in the following pharmacological test examples.

15 Pharmacological Test Example 1 (test of inhibition of NPY binding)

[0118] cDNA Sequence encoding a human NPY Y5 receptor [International Publication WO 96/16542] was cloned into expression vectors pcDNA3, pRc/RSV (manufactured by Invitrogen) and pCI-neo (manufactured by Promega). Using the cationic lipid method [see Proceedings of the National Academy of Science of the United States of America, vol.84, 20 p.7413 (1987)], host cells COS-7, CHO and LM(tk-) (American Type Culture Collection) were transfected with the thus prepared expression vectors to obtain cells in which the NPY Y5 receptor had been expressed.

25 [0119] Each of the membrane preparations thus prepared from the cells in which the NPY Y5 receptor had been expressed was incubated together with each compound to be tested and 20,000 cpm of [¹²⁵I] peptide YY (manufactured by Amersham) at 25°C for 2 hours in an assay buffer solution (25 mM HEPES buffer, pH 7.4, containing 10 mM magnesium chloride, 1 mM phenylmethylsulfonyl fluoride and 0.1% bacitracin) and then, the reaction mixture was filtered through a glass filter GF/C. After washing with 50 mM Tris buffer, pH 7.4, containing 0.3% BSA, radioactivity on the glass filter was measured using a gamma counter. Non-specific binding was measured in the presence of 1 µM of peptide YY to calculate a concentration of each compound tested which is needed to inhibit 50% of the specific binding to the peptide YY (IC₅₀ value) [see Endocrinology, vol.131, p.2090 (1992)]. As the result, IC₅₀ value of the compound of Example 30 was calculated to be 2.5 nM.

30 [0120] As shown in the above, the compound of the present invention strongly inhibited the binding of the peptide YY (a homologue of NPY) to the NPY Y5 receptor.

Pharmacological Test Example 2 (test of inhibition of feeding behavior induced by bPP)

35 [0121] Under pentobarbital anesthesia (single intraperitoneal injection of 50 mg/kg), a chronic guide cannula (outer diameter 0.8 mm; inner diameter 0.5 mm; length 10 mm) was stereotactically inserted in a right lateral cerebral ventricle of each of SD male rats (7 to 8-week-old, 200 to 300 g) and fixed using a dental resin. A tip of the guide cannula was positioned 0.9 mm behind a bregma, 1.2 mm at the right of a median line and in the depth of 1.5 mm from the brain surface. An inner needle was inserted such that its tip projected from the tip of the guide cannula by about 2 mm and arrived to a lateral cerebral ventricle. After a recovery period of about one week, a bovine pancreatic polypeptide (bPP, 5 µg/head/10 µl) was administered to the lateral cerebral ventricle. A compound to be tested was simultaneously administered as a mixture with bPP. Food intake during 2 hours from the administration was measured. In this connection, both bPP and the compound to be tested were administered after dissolving them in 50 % propylene glycol.

45 [0122] The compound of the present invention significantly inhibits the increase in food intake induced by bPP (a homologue of NPY) simultaneously administered.

[0123] In consequence, the compound [I] of the present invention is useful as an agent for the treatment of various diseases associated with NPY, for example, diseases of circulatory organs such as hypertension, nephropathy, cardiopathy and angiospasm, diseases of central nervous system such as bulimia, depression, epilepsy and dementia, metabolic diseases such as obesity, diabetes and dysendocrinosis, or glaucoma, especially bulimia, obesity and diabetes.

50 [0124] The compound represented by the general formula [I] can be administered orally or parenterally and by formulating into any dosage form suitable for such an administration, it can be used as an agent for the treatment of the diseases of circulatory organs such as hypertension, nephropathy, cardiopathy and angiospasm, the diseases of central nervous system such as bulimia, depression, epilepsy and dementia, the metabolic diseases such as obesity, diabetes and dysendocrinosis, or glaucoma. In clinical use of the compound of the present invention, it is also possible to administer the compound after formulating it into various dosage forms by adding any pharmaceutically acceptable additive(s). Examples of such additive include those which are generally used in the field of pharmaceuticals such as gelatin, lactose, sucrose, titanium oxide, starch, crystalline cellulose, hydroxypropylmethyl cellulose, carboxymethyl cel-

lulose, corn starch, microcrystalline wax, white soft paraffine, magnesium aluminate methasilicate, anhydrous calcium phosphate, citric acid, trisodium citrate, hydroxypropyl cellulose, sorbitol, sorbitan fatty acid ester, polysorbate, sucrose fatty acid ester, polyoxyethylene hydrogenated castor oil, polyvinyl pyrrolidone, magnesium stearate, light anhydrous silicic acid, talc, vegetable oil, benzyl alcohol, gum arabic, propylene glycol, polyalkylene glycol, cyclodextrin and hydroxypropyl cyclodextrin.

[0125] Examples of the dosage form to be formulated as a mixture with these additives include solid preparations such as tablet, capsule, granule, powder or suppository; and liquid preparations such as syrup, elixir or injection, which can be prepared in accordance with any conventional method in the field of pharmaceuticals. In this connection, in the case of the liquid preparation, it may be in a form which is dissolved or suspended in water or other suitable solvent when used. Also, particularly in the case of an injection, it may be dissolved or suspended in physiological saline or glucose solution if necessary or further mixed with buffer and/or preservative.

[0126] The pharmaceutical preparation may contain the compound of the present invention in an amount of from 1.0 to 100% by weight, preferably from 1.0 to 60% by weight, with respect to the total preparation. These pharmaceutical preparations may also contain any other therapeutically effective compounds.

[0127] When the compound of the present invention is, for example, clinically used, its dosage and the number of times of its administration vary depending on the sex, age, body weight and the conditions of each patient and the nature and ranges of the intended therapeutic effects and the like. When it is administered to an adult, it is desirable in general to orally administer in an amount of from 0.1 to 100 mg/kg per day by dividing the daily dose into 1 to several times per day, or to parenterally administer in an amount of from 0.001 to 10 mg/kg by dividing the daily dose into 1 to several times per day.

BEST MODE FOR CARRYING OUT THE INVENTION

[0128] The present invention is described further in detail with reference to the following examples, but the invention should in no way be restricted thereby.

Example 1

Preparation of 3-(2-indanyl)carbonylamino-5-(4-methylphenyl)pyrazole

[0129] 3-Amino-5-(4-methylphenyl)pyrazole (35 mg) and indan-2-carboxylic acid (33 mg) were dissolved in pyridine (2 ml) to which was subsequently added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (58 mg), and the mixture was stirred at room temperature overnight. The reaction solution was diluted with ethyl acetate (30 ml), washed with water (30 ml), saturated aqueous sodium bicarbonate (30 ml) and saturated brine (30 ml) and then dried over anhydrous magnesium sulfate. Then, the solvent was distilled away. The resulting crystalline residue was washed with ethyl ether to obtain the title compound (34 mg) as white crystals (melting point: 220 - 225°C).

[0130] Each of compounds of Examples 2 to 32 was obtained in the same manner as that described in Example 1 except that the starting materials used in Example 1 were replaced with appropriate starting materials corresponding to the desired compound.

Example 2

3-(2-indanyl)carbonylamino-5-(3-methylphenyl)pyrazole

[0131]

melting point: 85 - 87°C

Example 3

3-(2-indanyl)carbonylamino-5-(2-methylphenyl)pyrazole

[0132]

melting point: 148 - 152°C

Example 4

5-(4-chlorophenyl)-3-(1-indanyl)carbonylaminopyrazole

5 [0133]

melting point: 240 - 245°C

Example 5

10 3-(2-indanyl)carbonylamino-5-(3-methoxyphenyl)pyrazole

[0134]

15 melting point: 193 - 194°C

Example 6

20 5-(3-chlorophenyl)-3-(2-indanyl)carbonylaminopyrazole

[0135]

melting point: 200 - 203°C

25 Example 7

5-(3,4-dichlorophenyl)-3-(2-indanyl)carbonylaminopyrazole

[0136]

30 melting point: 238 - 240°C

Example 8

35 3-(2-indanyl)carbonylamino-5-(4-methoxyphenyl)pyrazole

[0137]

melting point: 199 - 203°C

40 Example 9

3-(2-indanyl)carbonylamino-5-(2-pyridyl)pyrazole

45 [0138]

melting point: 250 - 253°C

Example 10

50 3-(2-indanyl)carbonylamino-5-(4-pyridyl)pyrazole

[0139]

55 melting point: 259 - 261°C

Example 11

3-(2-indanyl)carbonylamino-5-(2-methoxyphenyl)pyrazole

5 [0140]

melting point: 217 - 220°C

Example 12

10 5-(4-chlorophenyl)-3-(1,2,3,4-tetrahydro-1-naphthyl)carbonylaminopyrazole

[0141]

15 melting point: 98 - 102°C

Example 13

20 5-(2-chlorophenyl)-3-(2-indanyl)carbonylaminopyrazole

[0142]

melting point: 175 - 178°C

25 Example 14

3-(2-indanyl)carbonylamino-5-(3-pyridyl)pyrazole

[0143]

30 melting point: 252 - 255°C

Example 15

35 3-(2-indanyl)carbonylamino-5-(1-naphthyl)pyrazole

[0144]

melting point: 107 - 112°C

40 Example 16

3-(2-indanyl)carbonylamino-5-(2-naphthyl)pyrazole

45 [0145]

melting point: 208 - 211°C

Example 17

50 5-(4-dimethylaminophenyl)-3-(2-indanyl)carbonylaminopyrazole

[0146]

55 melting point: 190 - 192°C

Example 18

5-(3-dimethylaminophenyl)-3-(2-indanyl)carbonylaminopyrazole

5 [0147]

melting point: 145 - 149°C (hydrochloride)

Example 19

5-(3,4-dimethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole

10 [0148]

15 melting point: 195 - 197°C

Example 20

3-(2-indanyl)carbonylamino-5-(4-isopropoxypyhenyl)pyrazole

20 [0149]

melting point: 194 - 195°C

25 Example 21

5-(4-ethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole

30 [0150]

35 melting point: 204 - 206°C

Example 22

3-(2-indanyl)carbonylamino-5-(4-trifluoromethylphenyl)pyrazole

35 [0151]

40 melting point: 285 - 287°C

Example 23

3-(2-indanyl)carbonylamino-5-(3-trifluoromethylphenyl)pyrazole

45 [0152]

melting point: 195 - 197°C

Example 24

3-(2-indanyl)carbonylamino-5-(4-methylthiophenyl)pyrazole

50 [0153]

55 melting point: 215 - 217°C

Example 253-(2-indanyl)carbonylamino-5-(3,4-methylenedioxophenyl)pyrazole

5 [0154]

melting point: 197 - 201°C

Example 265-(3-dimethylamino-4-methoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole

10 [0155]

15 $^1\text{H-NMR}(\text{CDCl}_3)$ δ: 2.78 (6H, s), 3.1 - 3.4 (5H, m), 3.87 (3H, s), 6.8 - 6.9 (2H, m), 7.1 - 7.2 (6H, m), 8.59 (1H, brs)Example 273-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole

20 [0156]

melting point: 264 - 269°C

25 Example 285-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydro-2-naphthyl)carbonylaminopyrazole

30 [0157]

35 $^1\text{H-NMR}(\text{CDCl}_3)$ δ: 1.91 - 2.17 (2H, m), 2.57 - 3.14 (5H, m), 3.86 (3H, s), 3.87 (3H, s), 6.82 - 6.86 (2H, m), 7.05 - 7.26 (6H, m), 8.69 (1H, brs)Example 293-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole

40 [0158]

45 $^1\text{H-NMR}(\text{CDCl}_3)$ δ: 3.11 - 3.25 (1H, m), 3.30 - 3.55 (4H, m), 3.72 (3H, s), 3.76 (3H, s), 6.64 (1H, d, J=8.4 Hz), 6.84 (1H, s), 7.03 (1H, dd, J=1.8 Hz & 8.1 Hz), 7.07 (1H, s), 7.18 (1H, d, J=8.4 Hz), 7.32 - 7.40 (2H, m), 7.54 - 7.59 (2H, m), 7.23 - 7.76 (1H, m), 9.13 (1H, s)Example 303-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole

45 [0159]

50 melting point: 270 - 275°C

Example 315-(4-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole

55 [0160]

melting point: 267 - 269°C

Example 325-(3-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole

5 [0161]

melting point: 197 - 200°C

Example 33Preparation of 3-(2-indanyl)carbonylamino-5-(4-vinylphenyl)pyrazole

[0162] 5-(4-Bromophenyl)-3-(2-indanyl)carbonylaminopyrazole (106.5 mg), tributylvinyltin (0.25 ml), a tris(dibenzylideneacetone)dipalladium chloroform complex (17.1 mg), tri-2-furylphosphine (34.4 mg) and lithium chloride (34.0 mg) were dissolved in N-methylpyrrolidone (2 ml) with heating, and the resultant mixture was heated at 80°C overnight. After allowing to cool, the reaction solution was diluted with ethyl acetate-hexane (1:1, 100 ml), washed with saturated aqueous potassium fluoride solution (100 ml x 2) and then dried over anhydrous magnesium sulfate. The solvent was distilled away under a reduced pressure. The resultant residue was purified by column chromatography on silica gel (ethyl acetate:hexane = 1:1) and then crystallized from chloroform to obtain the title compound (70.2 mg) as white crystals (melting point: 193 - 195°C).

Example 34Preparation of 3-(2-indanyl)carbonylamino-5-(3-vinylphenyl)pyrazole

[0163] The title compound was prepared in the same manner as that described in Example 33 except that 5-(4-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole used in Example 33 was replaced with 5-(3-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole.

30 ¹H-NMR (CDCl₃) δ: 3.22-3.40 (5H, m), 5.31 (1H, dd, J=0.6 Hz & 10.9 Hz), 5.80 (1H, dd, J=0.6 Hz & 17.6 Hz), 6.73 (1H, dd, J=10.9 Hz & 17.6 Hz), 6.88 (1H, s), 7.15 - 7.50 (7H, m), 7.64 (1H, s), 8.18 (1H, s)

Example 35Preparation of 3-(2-indanyl)carbonylamino-5-(4-(2-propenyl)phenyl)pyrazole

[0164] The title compound was prepared in the same manner as that described in Example 33 except that tributylvinyltin used in Example 33 was replaced with allyltributyltin.

40 melting point: 210 - 212°C

Example 36Preparation of 5-(4-biphenylyl)-3-(2-indanyl)carbonylaminopyrazole

[0165] The title compound was prepared in the same manner as that described in Example 33 except that tributylvinyltin used in Example 33 was replaced with tributylphenyltin.

50 melting point: 228 - 230°C

Example 37Preparation of 5-(3-biphenylyl)-3-(2-indanyl)carbonylaminopyrazole

[0166] The title compound was prepared in the same manner as that described in Example 33 except that 5-(4-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole and tributylvinyltin used in Example 33 were replaced with 5-(3-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole and tributylphenyltin, respectively.

melting point: 108 - 110°C

Example 38

5 Preparation of 5-(4-ethylphenyl)-3(2-indanyl)carbonylaminopyrazole

[0167] 3-(2-Indanyl)carbonylamino-5-(4-vinylphenyl)pyrazole (25.0 mg) was dissolved in ethanol (5.0 ml) to which was subsequently added 10 % palladium-carbon (22 mg), and then the mixture was stirred under hydrogen atmosphere of 1 atmospheric pressure overnight. The catalyst was filtered off and then, the filtrate was concentrated under a reduced pressure to obtain the title compound (24.8 mg) as colorless crystals (melting point: 196- 198°C).

Example 39

15 Preparation of 5-(3-ethylphenyl)3-(2-indanyl)carbonylaminopyrazole

[0168] The title compound was prepared in the same manner as that described in Example 38 except that 3-(2-indanyl)carbonylamino-5-(4-vinylphenyl)pyrazole used in Example 38 was replaced with 3-(2-indanyl)carbonylamino-5-(3-vinylphenyl)pyrazole.

20 ¹H-NMR (CDCl₃) δ: 1.23 (3H, t, J=7.7 Hz), 2.64 (2H, q, J=7.7 Hz), 3.15 - 3.35 (5H, m), 6.90 (1H, s), 7.12 - 7.42 (8H, m), 8.67 (1H, s)

Example 40

25 Preparation of 3-(2-indanyl)carbonylamino-5-(4-propylphenyl)pyrazole

[0169] The title compound was prepared in the same manner as that described in Example 38 except that 3-(2-indanyl)carbonylamino-5-(4-vinylphenyl)pyrazole used in Example 38 was replaced with 3-(2-indanyl)carbonylamino-5-(4-(2-propenyl)phenyl)pyrazole.

30 melting point: 211- 213°C

Example 41

35 Preparation of 5-(4-methoxyphenyl)-3-(2-methyl-2-indanyl)carbonylaminopyrazole

[0170] 2-Methylindan-2-carboxylic acid (100 mg) was dissolved in thionyl chloride (0.57 ml) and the mixture was heated under reflux for 3 hours. The reaction solution was concentrated under a reduced pressure. To the resultant residue was added toluene and then, the solvent was distilled away. The residue was dissolved in pyridine (1 ml) to which was subsequently added 3-amino-5-(4-methoxyphenyl)pyrazole (108 mg). The mixture was stirred at room temperature overnight. The reaction solution was concentrated under a reduced pressure. The resultant residue was partitioned between chloroform and saturated aqueous sodium bicarbonate - The organic layer was taken off, from which the solvent was distilled away under a reduced pressure. The resultant residue was purified by column chromatography on silica gel (ethyl acetate : hexane = 5:5 → 7:3) to obtain the title compound (125 mg) as colorless crystals (melting point: 45 171 - 172°C).

[0171] Each of compounds of Examples 42 to 72 was obtained in the same manner as that described in Example 1 except that the starting materials were replaced with appropriate starting materials corresponding to the desired compound.

50 Example 42

3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylaminopyrazole

[0172]

55 ¹H-NMR (CDCl₃) δ: 3.40-3.65 (5H, m), 6.68 (1H, s), 7.33 (1H, d, J=8.4 Hz), 7.40 - 7.50 (2H, m), 7.54 (2H, d, J=6.3 Hz), 7.71 (2H, t, J=7.5 Hz), 7.83 (1H, d, J=7.5 Hz), 8.60 (2H, d, J=5.7 Hz), 8.65 (1H, s)

Example 43(+)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole

5 [0173]

¹H-NMR (CDCl₃) δ: 3.40 - 3.65 (5H, m), 6.68 (1H, s), 7.33 (1H, d, J=8.4 Hz), 7.40 - 7.50 (2H, m), 7.54 (2H, d, J=6.3 Hz), 7.71 (2H, t, J=7.5 Hz), 7.83 (1H, d, J=7.5 Hz), 8.60 (2H, d, J=5.7 Hz), 8.65 (1H, s)
 $[\alpha]_D^{20} = +108^\circ$ (c=0.1, DMSO)

10 Example 44

(-)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole

15 [0174]

¹H-NMR (CDCl₃) δ: 3.40 - 3.65 (5H, m), 6.68 (1H, s), 7.33 (1H, d, J=8.4 Hz), 7.40 - 7.50 (2H, m), 7.54 (2H, d, J=6.3 Hz), 7.71 (2H, t, J=7.5 Hz), 7.83 (1H, d, J=7.5 Hz), 8.60 (2H, d, J=5.7 Hz), 8.65 (1H, s)
 $[\alpha]_D^{20} = -108^\circ$ (c=0.1, DMSO)

20 Example 45

3-(5,6-dichloroindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole

25 [0175]

melting point: 260 - 261°C

Example 463-(5-chloroindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole

30 [0176]

melting point: 194 - 197°C

Example 473-(5,6-dichloroindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole

40 [0177]

melting point: 278 - 280°C

Example 483-(4-bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole

45 [0178]

melting point: 93 - 95°C

Example 493-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole

5 [0179]

melting point: 135 - 139°C

Example 503-(5-bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole

10 [0180]

15 melting point: 207 - 209°C

Example 515-(4-methoxyphenyl)-3-(4-phenylindan-2-yl)carbonylaminopyrazole

20 [0181]

melting point: 110 - 115°C

25 Example 523-(4-phenylindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole

30 [0182]

melting point: 110 - 115°C

Example 5335 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole

[0183]

40 ¹H-NMR (DMSO-d₆) δ: 1.24 (3H, t, J=7.6 Hz), 2.76 (2H, q, J=7.6 Hz), 3.21 - 3.67 (5H, m), 7.14 (1H, s), 7.39 - 7.58 (4H, m), 7.59 (1H, s), 7.74 - 7.81 (2H, m), 7.90 (1H, d, J=8.3 Hz), 8.48 (1H, d, J=4.9 Hz), 10.73 (1H, s), 13.15 (1H, s)Example 54(+)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole

45 [0184]

50 ¹H-NMR (DMSO-d₆) δ: 1.24 (3H, t, J=7.6 Hz), 2.76 (2H, q, J=7.6 Hz), 3.21 - 3.67 (5H, m), 7.14 (1H, s), 7.39 - 7.58 (4H, m), 7.59 (1H, s), 7.74 - 7.81 (2H, m), 7.90 (1H, d, J=8.3 Hz), 8.48 (1H, d, J=4.9 Hz), 10.73 (1H, s), 13.15 (1H, s)
[α]_D²⁰ = +92° (c=0.1, DMSO)Example 55(-)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole

55 [0185]

¹H-NMR (DMSO-d₆) δ: 1.24 (3H, t, J=7.6 Hz), 2.76 (2H, q, J=7.6 Hz), 3.21 - 3.67 (5H, m), 7.14 (1H, s), 7.39 - 7.58

(4H, m), 7.59 (1H, s), 7.74 - 7.81 (2H, m), 7.90 (1H, d, J=8.3 Hz), 8.48 (1H, d, J=4.9 Hz), 10.73 (1H, s), 13.15 (1H, s)
 $[\alpha]_D^{20} = -112^\circ$ (c=0.1, DMSO)

Example 56

5

3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-methylpyridin-4-yl)pyrazole

[0186]

10

¹H-NMR (CDCl₃) δ: 2.51 (3H, s), 3.30 - 3.62 (5H, m), 6.72 (1H, s), 7.27 (2H, d, J=6.9 Hz), 7.31 - 7.47 (3H, m), 7.63
 - 7.66 (2H, m), 7.80 (1H, d, J=7.2 Hz), 8.42 (1H, d, J=5.0 Hz), 8.96 (1H, s)

Example 57

15

3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-propylpyridin-4-yl)pyrazole

[0187]

20

¹H-NMR (DMSO-d₆) δ: 0.90 (3H, t, J=7.4 Hz), 1.71 (2H, sext, J=7.4 Hz), 2.71 (2H, t, J=7.4 Hz), 3.31 - 3.68 (5H, m),
 7.16 (1H, s), 7.40 - 7.54 (4H, m), 7.58 (1H, s), 7.73 - 7.81 (2H, m), 7.90 (1H, d, J=7.8 Hz), 8.49 (1H, d, J=5.3 Hz),
 10.75 (1H, s), 13.16 (1H, s)

Example 58

25

5-(2-butylpyriain-4-yl)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylaminopyrazole

[0188]

30

¹H-NMR (DMSO-d₆) δ: 0.91 (3H, t, J=7.4 Hz), 1.26 - 1.39 (2H, m), 1.63 - 1.73 (2H, m), 2.75 (2H, t, J=7.6 Hz), 3.29
 - 3.68 (5H, m), 7.15 (1H, s), 7.41 - 7.59 (5H, m), 7.75 - 7.83 (2H, m), 7.92 (1H, d, J=7.9 Hz), 8.49 (1H, d, J=4.8 Hz),
 10.74 (1H, s), 13.15 (1H, s)

Example 59

35

3-(bicyclo[4.2.0]oct-1(6).2,4-trien-7-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole

[0189]

40

¹H-NMR (DMSO-d₆) δ: 2.82 - 2.86 (1H, m), 4.17 (3H, s), 4.21 (3H, s), 4.66 - 4.71 (1H, m), 4.82 - 4.86 (1H, m), 7.19
 (1H, s), 7.38 - 7.81 (7H, m), 8.98 (1H, s), 12.96 (1H, s)

Example 60

45

5-(4-methoxyphenyl)-3-(5-nitroindan-2-yl)carbonylaminopyrazole

[0190]

melting point: 191 - 193°C

50

Example 615-(4-methoxyphenyl)-3-(4-nitroindan-2-yl)carbonylaminopyrazole

[0191]

55

melting point: 115 - 118°C

Example 625-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrocarbazol-2-yl)carbonylaminopyrazole

5 [0192]

melting point: 256 - 258°C

Example 633-(5-benzoylindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole

10 [0193]

15 melting point: 190 - 195°C

Example 643-(5-benzoylindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole

20 [0194]

melting point: 121 - 125°C

25 Example 655-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrodibenzo[b,d]furan-3-yl)carbonylaminopyrazole

30 [0195]

¹H-NMR (CDCl₃) δ: 1.95 - 2.08 (1H, m), 2.20 - 2.30 (1H, m), 2.52 - 2.66 (1H, m), 2.72 - 2.88 (2H, m), 2.94 - 3.20 (2H, m), 3.87 (3H, s), 3.89 (3H, s), 6.83 (1H, d, J=8.1 Hz), 6.89 (1H, s), 7.07 - 7.23 (4H, m), 7.36 - 7.41 (2H, m), 8.62 (1H, s)

35 Example 665-(3,4-dimethoxyphenyl)-3-(9-methyl-1,2,3,4-tetrahydrocarbazol-2-yl)carbonylaminopyrazole

40 [0196]

¹H-NMR (DMSO-d₆) δ: 1.73 - 1.89 (1H, m), 2.10 - 2.20 (1H, m), 2.55 - 3.00 (5H, m), 3.62 (3H, s), 3.78 (3H, s), 3.82 (3H, s), 6.83 - 7.09 (4H, m), 7.23 - 7.38 (4H, m), 10.55 (1H, s), 12.67 (1H, s)

45 Example 673-(2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole

50 [0197]

melting point: 255 - 257°C

Example 683-(2,3-dihydro-1H-cyclopenta[b]indol-2-yl)-5-(4-methoxyphenyl)carbonylaminopyrazole

55 [0198]

¹H-NMR (DMSO-d₆) δ: 2.90 (1H, dd, J=6.5 & 14.1 Hz), 3.00 - 3.19 (3H, m), 3.78 (3H, s), 3.89 (1H, m), 6.82 (1H,

s), 6.88 - 7.04 (4H, m), 7.24 - 7.34 (2H, m), 7.60 - 7.70 (2H, m), 10.53 (1H, s), 10.82 (1H, s), 12.63 (1H, s)

Example 69

5 3-(7,8-dihydro-6H-cyclopenta[g]quinolin-7-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole

[0199]

10 ¹H-NMR (DMSO-d₆) δ: 3.27 - 3.49 (4H, m), 3.51 - 3.78 (1H, m), 3.78 (3H, s), 6.83 (1H, s), 6.99 (2H, d, J=8.7 Hz),
7.41 - 7.45 (1H, m), 7.64 (2H, d, J=8.7 Hz), 7.77 (1H, s), 7.82 (1H, s), 8.25 (1H, d, J=7.5 Hz), 8.78 - 8.80 (1H, m),
10.62 (1H, s), 12.67 (1H, s)

Example 70

15 5-(2-ethylpyridin-4-yl)-3-(2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)carbonylaminopyrazole

[0200]

20 ¹H-NMR (CDCl₃) δ: 1.21 (3H, t, J=7.6 Hz), 2.74 (2H, q, J=7.6 Hz), 3.16 - 3.33 (2H, m), 3.66 - 3.74 (1H, m), 4.11 -
4.28 (2H, m), 6.10 (1H, s), 6.83 (1H, s), 7.01 - 7.13 (3H, m), 7.21 (1H, d, J=5.1 Hz), 7.35 (1H, s), 7.49 (1H, d, J=6.9
Hz), 8.36 (1H, d, J=5.1 Hz), 9.47 (1H, s)

Example 71

25 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrodibenzo[b,d]thiophen-3-yl)carbonylaminopyrazole

[0201]

30 melting point: 222 - 224°C

Example 72

5-(4-methoxyphenyl)-3-(4-methyl-2,3-dihydro-1H-cyclopenta[b]indol-2-yl)carbonylaminopyrazole

35 [0202]

30 ¹H-NMR (CDCl₃) δ: 3.04 - 3.40 (4H, m), 3.61 (3H, s), 3.80 (1H, m), 3.81 (3H, s), 6.82 (1H, s), 6.90 (2H, d, J=8.9
Hz), 7.04 - 7.31 (3H, m), 7.40 (1H, m), 7.45 (2H, d, J=8.9 Hz), 8.64 (1H, s)

40 Example 73

Preparation of 5-(4-methoxyphenyl)3-(5-phenylindan-2-yl)carbonylaminopyrazole.

45 [0203] 3-(5-Bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole (50 mg), tributylphenyltin (0.12 ml), a
tris(dibenzylideneacetone)dipalladium chloroform complex (6 mg), tri-2-furylphosphine (11 mg) and lithium chloride (25
mg) were dissolved in N-methylpyrrolidone (1 ml) with heating, and the mixture was heated at 85°C overnight. After
allowing to cool, the reaction solution was concentrated under a reduced pressure. The residue was dissolved in ethyl
acetate-hexane (1:1, 30 ml) and the solution was washed with saturated aqueous potassium fluoride solution and dried
over anhydrous magnesium sulfate. The solvent was distilled away under a reduced pressure. The resultant residue
50 was purified by preparative thin layer chromatography (chloroform: methanol = 20:1) to obtain the title compound (4.4
mg).

55 ¹H-NMR (CDCl₃) δ: 3.28 - 3.42 (5H, m), 3.83 (3H, s), 6.83 (1H, brs), 6.93 (2H, d, J=8.8 Hz), 7.28 - 7.34 (2H, m),
7.39 - 7.44 (4H, m), 7.52 - 7.57 (4H, m)

Reference Example 1Preparation of 3-amino-5-(3,4-dimethoxyphenyl)pyrazole

5 (1) Preparation of 3,4-dimethoxybenzoylacetoneitrile

[0204] Dry acetonitrile (1.8 ml) was added to a solution of n-butyl lithium (a 2.5M solution in hexane, 13.8 ml) in dry THF (30 ml) at -78°C and the mixture was stirred at the same temperature for 1 hour to which was subsequently added a solution of methyl 3,4-dimethoxybenzoate (6.42 g) in dry THF (15 ml). The mixture was stirred at -78°C for 3 hours and then at room temperature for 1 hour. Water (100 ml) was added to the reaction solution and the resultant mixture was extracted with ethyl ether (100 ml). After the aqueous layer was acidified with 6 N hydrochloric acid, it was extracted with ethyl acetate (200 ml x 3). The organic layers were combined, washed with saturated brine and then dried over anhydrous sodium sulfate. Then, the solvent was distilled away under a reduced pressure. The resultant residue was crystallized from ethyl acetate-hexane to obtain the title compound (3.6 g) as pale yellow crystals.

15 ¹H-NMR(CDC₁₃) δ: 3.95 (3H, s), 3.97 (3H, s), 4.03 (2H, s), 6.92 (1H, d, J=9.0 Hz), 7.49 (1H, d, J=9.0 Hz), 7.51 (1H, s)

20 (2) Preparation of 3-amino-5-(3,4-dimethoxyphenyl)pyrazole

[0205] 3,4-Dimethoxybenzoylacetoneitrile (3.6 g) was dissolved in ethanol (20 ml) to which was subsequently added hydrazine monohydrate (0.87 ml) under cooling with ice. The mixture was heated under reflux for 7 hours and allowed to cool. Then, the solvent was distilled away under a reduced pressure. The resultant residue was recrystallized from ethyl acetate to obtain the title compound (2.92 g) as colorless crystals (melting point: 124 - 125°C).

25 [0206] Each of the following compounds was obtained in the same manner as that described in the above except that methyl 3,4-dimethoxybenzoate used in the above reaction was replaced with an appropriate compound corresponding to the desired compound:

3-amino-5-(3-chlorophenyl)pyrazole

30 [0207]

melting point: 103-104°C;

35 3-amino-5-(3,4-dichlorophenyl)pyrazole

[0208]

melting point: 169-170°C;

40 3-amino-5-(4-dimethylaminophenyl)pyrazole

[0209]

45 melting point: 215-218°C (decomposition);

3-amino-5-(3-dimethylaminophenyl)pyrazole (dihydrochloride)

[0210]

50 melting point: 195-200°C (decomposition);

3-amino-5-(4-isopropoxyphenyl)pyrazole

55 [0211]

melting point: 160-165°C;

3-amino-5-(3-bromophenyl)pyrazole

[0212]

5 melting point: 126-130°C;

3-amino-5-(4-methylthiophenyl)pyrazole

[0213]

10 melting point: 150-156°C;

3-amino-5-(3,4-methylenedioxyphenyl)pyrazole

15 [0214]

melting point: 134-136°C;

3-amino-5-(3-dimethylamino-4-methoxyphenyl)pyrazole

20 [0215]

melting point: 158-160°C;

25 3-amino-5-(1-naphthyl)pyrazole

[0216]

melting point: 165-168°C;

30 3-amino-5-(2-naphthyl)pyrazole

[0217]

35 melting point: 125-132°C;

3-amino-5-(3-trifluoromethylphenyl)pyrazole

[0218]

40 melting point: 122 - 128°C;

3-amino-5-(2-ethylpyridin-4-yl)pyrazole

45 [0219]

1H-NMR (CDCl₃) δ: 1.26 (3H, t, J=7.5 Hz), 2.79 (2H, q, J=7.5 Hz), 5.10 - 5.90 (2H, brs), 5.98 (1H, s), 7.24 - 7.28 (1H, m), 7.32 (1H, s), 8.44 - 8.47 (1H, m);

50 3-amino-5-(2-propylpyridin-4-yl)pyrazole

[0220]

55 1H-NMR(CDCl₃) δ: 0.96 (3H, t, J=7.3 Hz), 1.68 - 1.84 (2H, m), 2.77 (2H, q, J=7.6 Hz), 3.50 - 4.60 (2H, brs), 6.01 (1H, s), 7.24 - 7.28 (1H, m), 7.31 (1H, s), 8.51 (1H, d, J=5.1 Hz);

3-amino-5-(2-butylpyridin-4-yl)pyrazole

[0221]

5 ¹H-NMR(CDCI₃) δ: 0.91 (3H, t, J=7.3 Hz), 1.29 - 1.41 (2H, m), 1.61 - 1.72 (2H, m), 2.75 (2H, q, J=7.6 Hz), 3.50 - 4.50 (2H, brs), 5.99 (1H, s), 7.24 - 7.28 (1H, m), 7.30 (1H, s), 8.49 (1H, d, J=4.8 Hz)

Reference Example 2

10 Preparation of 2-indancarboxylic acid derivatives

[0222] The following 2-indancarboxylic acid derivatives were synthesized according to the method as described in the literature (Journal of American Chemical Society, Vol.97, page 347 (1975):

15 4-bromo-2-indancarboxylic acid

[0223]

melting point: 82-89°C;

20 5-chloro-2-indancarboxylic acid

[0224]

25 ¹H-NMR (DMSO-d₆) δ: 3.05 - 3.17 (4H, m), 3.20 - 3.39 (1H, m), 7.13 - 7.30 (3H, m);

5,6-dichloro-2-indancarboxylic acid

[0225]

30 melting point: 162 - 167°C;

2,3-dihydro-1H-cyclopenta[a]naphthalene-2-carboxylic acid

35 [0226]

1H-NMR (CDCl₃) δ: 3.43 - 3.63 (5H, m), 7.35 - 7.55 (3H, m), 7.69 - 7.87 (3H, m);

2,3-dihydro-1H-cyclopenta[b]naphthalene-2-carboxylic acid

40 [0227]

melting point: 210-213°C

1H-NMR (CDCI₃) δ: 3.41 (5H, s), 7.40 (2H, dd, J=3.4 Hz & 6.1 Hz), 7.66 (2H,s), 7.76 (2H, dd, J=3.4 Hz & 6.1 Hz);

45 4-nitro-2-indancarboxylic acid

[0228]

50 melting point: 80-82°C;

5-nitro-2-indancarboxylic acid

[0229]

55 melting point: 65-69°C.

Reference Example 3Preparation of (-)-2,3-dihydro-1H-cyclopenta[a]naphthalene-2-carboxylic acid

- 5 [0230] 2,3-Dihydro-1H-cyclopenta[a]naphthalene-2-carboxylic acid (15.59 g) was dissolved in 1,4-dioxane to which was subsequently added (+)-1-(1-naphthyl)ethylamine (12.57 g) and then precipitated crystals were collected by filtration. The crystals were recrystallized from hot 1,4-dioxane and the resultant crystals were suspended in 1 N hydrochloric acid. The suspension was extracted with chloroform. The chloroform layer was concentrated under a reduced pressure to obtain the title compound (3.82 g) as white powders (melting point: 139 - 141°C; $[\alpha]_D^{20} = -95^\circ$ (c=1, CHCl₃)).
- 10 [0231] (+)-2,3-Dihydro-1H-cyclopenta[a]naphthalene-2-carboxylic acid was obtained in the same manner as that described above except that (+)-1-(1-naphthyl)ethylamine used was replaced with (-)-1-(1-naphthyl)ethylamine.

Reference Example 4

- 15 [0232] Preparation of 4-phenyl-2-indancarboxylic acid

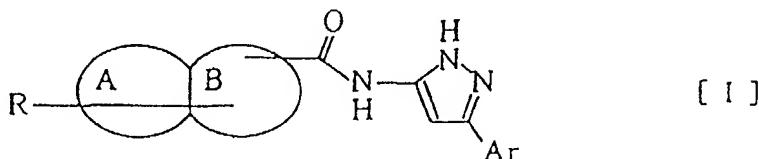
[0232] Methyl 4-bromo-2-indancarboxylate (510 mg), tributylphenyltin (881 mg), a tris(dibenzylideneacetone)dipalladium chloroform complex (41 mg) and tri-2-furylphosphine (19 mg) were dissolved in N-methylpyrrolidone (10 ml), and the mixture was stirred at 70°C for 3 hours and allowed to cool. To the reaction solution was added a saturated potassium fluoride solution and the solution was stirred at room temperature for 30 minutes followed by filtering through Celite. The filtrate was extracted with ether. The organic layers was washed with saturated aqueous sodium bicarbonate and saturated brine and then dried over anhydrous magnesium sulfate. Then, the solvent was distilled away under a reduced pressure. The resultant residue was purified by column chromatography on silica gel (hexane: ethyl acetate = 4 : 1) to obtain methyl 4-phenyl-2-indancarboxylate. The resultant ester was dissolved in methanol to which 1 N sodium hydroxide was added to hydrolyze. Methanol was distilled away under a reduced pressure. To the resultant residue was added 1 N hydrochloric acid. The product was extracted with ethyl acetate. The organic layer was washed with saturated brine and then dried over anhydrous magnesium sulfate. Then, the solvent was distilled away to obtain the title compound (351 mg) (melting point: 97 - 102°C).

30 **INDUSTRIAL APPLICABILITY**

[0233] Since the compound of the present invention has an antagonistic action to NPY, it is useful as an agent for the treatment of various diseases associated with NPY, for example, diseases of circulatory organs such as hypertension, nephropathy, cardiopathy and angospasm, diseases of central nervous system such as bulimia, depression, epilepsy and dementia, metabolic diseases such as obesity, diabetes and dysendocrinosis, or glaucoma.

35 **Claims**

- 40 1. A compound represented by the general formula [I]:



50 wherein A and B rings are ortho-condensed to each other, A ring represents an aromatic carbocyclic or heterocyclic ring and B ring represents an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed; Ar represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; and R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, provided that when the group represented by

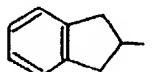
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is the group represented by

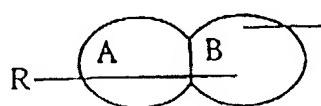
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15 Ar is not a phenyl group nor a 4-chlorophenyl group, or a salt thereof.

2. The compound as claimed in claim 1 wherein the group represented by the formula:

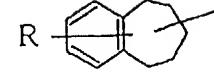
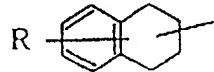
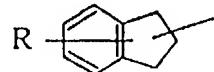
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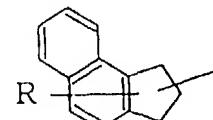
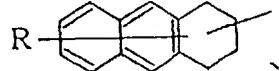
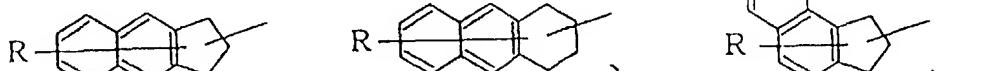
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is a group represented by the formula:

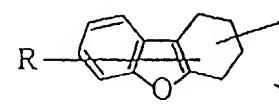
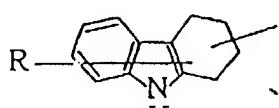
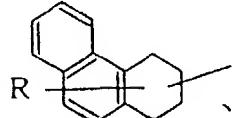
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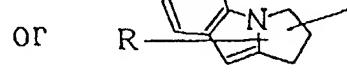
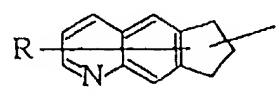
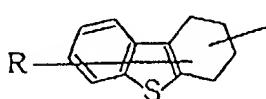
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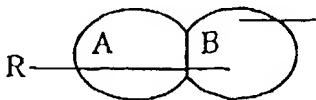


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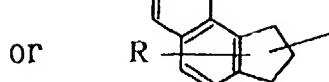
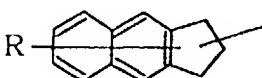
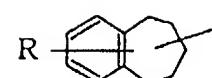
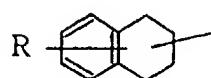
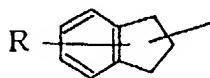
wherein R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

3. The compound as claimed in claim 1 wherein the group represented by the formula:

55

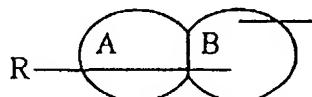


is a group represented by the formula:

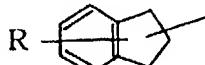


15 wherein R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

4. The compound as claimed in claim 1 wherein the group represented by the formula:



25 is a group represented by the formula:

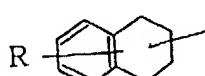


35 wherein R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

- 35 5. The compound as claimed in claim 1 wherein the group represented by the formula:



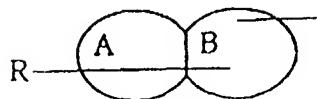
45 is a group represented by the formula:



55 wherein R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

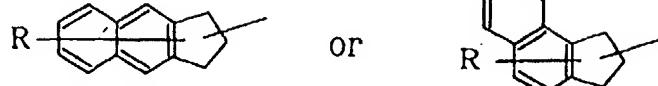
- 55 6. The compound as claimed in claim 1 wherein the group represented by the formula:

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is a group represented by the formula:

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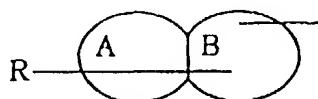
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wherein R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

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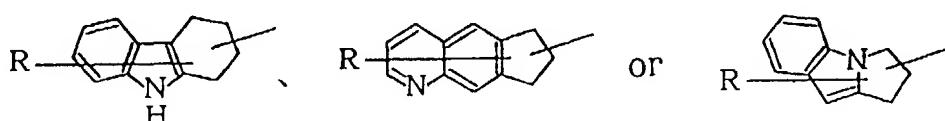
7. The compound as claimed in claim 1 wherein the group represented by the formula:

25



is a group represented by the formula:

30



35

wherein R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom.

40

8. The compound as claimed in claim 1 wherein the aromatic carbocyclic ring group as Ar is a phenyl group or a naphthyl group.

45

9. The compound as claimed in claim 1 wherein the aromatic heterocyclic ring group as Ar is a pyridyl group.

10. The compound as claimed in claim 1 which is

50

3-(2-indanyl)carbonylamino-5-(4-methylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(3-methylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(2-methylphenyl)pyrazole,
 5-(4-chlorophenyl)-3-(1-indanyl)carbonylamino pyrazole,
 3-(2-indanyl)carbonylamino-5-(3-methoxyphenyl)pyrazole,
 5-(3-chlorophenyl)-3-(2-indanyl)carbonylamino pyrazole,
 5-(3,4-dichlorophenyl)-3-(2-indanyl)carbonylamino pyrazole,
 3-(2-indanyl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(2-pyridyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(4-pyridyl)pyrazole,

55

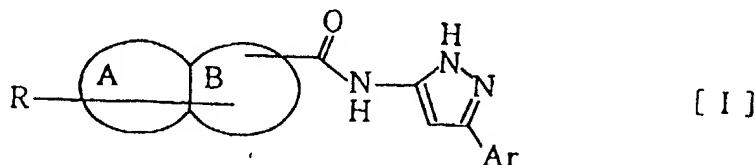
3-(2-indanyl)carbonylamino-5-(2-methoxyphenyl)pyrazole,
 5-(4-chlorophenyl)-3-(1,2,3,4-tetrahydro-1-naphthyl)carbonylaminopyrazole,
 5-(2-chlorophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5
 3-(2-indanyl)carbonylamino-5-(3-pyridyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(1-naphthyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(2-naphthyl)pyrazole,
 5-(4-dimethylaminophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-dimethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 10
 5-(3,4-dimethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-isopropoxyphenyl)pyrazole,
 5-(4-ethoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-trifluoromethylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(3-trifluoromethylphenyl)pyrazole,
 15
 3-(2-indanyl)carbonylamino-5-(4-methylthiophenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(3,4-methylenedioxypyphenyl)pyrazole,
 5-(3-dimethylamino-4-methoxyphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydro-2-naphthyl)carbonylaminopyrazole,
 20
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 5-(4-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-bromophenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-vinylphenyl)pyrazole,
 25
 3-(2-indanyl)carbonylamino-5-(3-vinylphenyl)pyrazole,
 3-(2-indanyl)carbonylamino-5-(4-(2-propenyl)phenyl)pyrazole,
 5-(4-biphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(3-biphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 5-(4-ethylphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 30
 5-(3-ethylphenyl)-3-(2-indanyl)carbonylaminopyrazole,
 3-(2-indanyl)carbonylamino-5-(4-propylphenyl)pyrazole,
 5-(4-methoxyphenyl)-3-(2-methyl-2-indanyl)carbonylaminopyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 (+)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 (-)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 35
 3-(5,6-dichloroindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(5-chloroindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(5,6-dichloroindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 3-(4-bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 40
 3-(5-bromoindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 5-(4-methoxyphenyl)-3-(4-phenylindan-2-yl)carbonylaminopyrazole,
 3-(4-phenylindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 (+)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 45
 (-)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-ethylpyridin-4-yl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-methylpyridin-4-yl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylamino-5-(2-propylpyridin-4-yl)pyrazole,
 5-(2-butylpyridin-4-yl)-3-(2,3-dihydro-1H-cyclopenta[a]naphthalen-2-yl)carbonylaminopyrazole,
 3-(bicyclo[4.2.0]oct-1(6),2,4-trien-7-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 50
 5-(4-methoxyphenyl)-3-(5-nitroindan-2-yl)carbonylaminopyrazole,
 5-(4-methoxyphenyl)-3-(4-nitroindan-2-yl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrocarbazol-2-yl)carbonylaminopyrazole,
 3-(5-benzoylindan-2-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 3-(5-benzoylindan-2-yl)carbonylamino-5-(4-pyridyl)pyrazole,
 55
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydronaphthalen-3-yl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(9-methyl-1,2,3,4-tetrahydrocarbazol-2-yl)carbonylaminopyrazole,
 3-(2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)carbonylamino-5-(3,4-dimethoxyphenyl)pyrazole,
 3-(2,3-dihydro-1H-cyclopenta[b]indol-2-yl)-5-(4-methoxyphenyl)carbonylaminopyrazole,

3-(7,8-dihydro-6H-cyclopenta[g]quinolin-7-yl)carbonylamino-5-(4-methoxyphenyl)pyrazole,
 5-(2-ethylpyridin-4-yl)-3-(2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)carbonylaminopyrazole,
 5-(3,4-dimethoxyphenyl)-3-(1,2,3,4-tetrahydrodibenzo[b,d]thiophen-3-yl)carbonylaminopyrazole,
 5-(4-methoxyphenyl)-3-(4-methyl-2,3-dihydro-1H-cyclopenta[b]indol-2-yl)carbonylaminopyrazole, or
 5-(4-methoxyphenyl)-3-(5-phenyliindan-2-yl)carbonylaminopyrazole.

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11. A method for preparing a compound represented by the general formula [I]:

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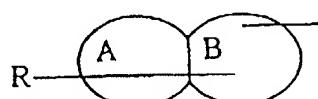
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wherein A and B rings are ortho-condensed to each other, A ring represents an aromatic carbocyclic or heterocyclic ring and B ring represents an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed; Ar represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; and R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, provided that when the group represented by

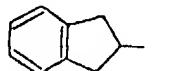
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is the group represented by

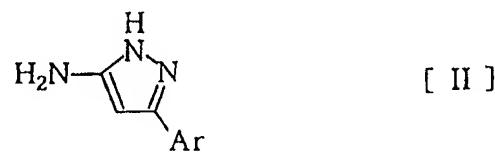
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Ar is not a phenyl group nor a 4-chlorophenyl group,
 or a salt thereof, which comprises reacting a compound represented by the general formula [II]:

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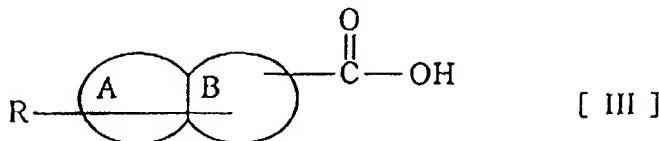


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wherein Ar is as defined above, with a carboxylic acid represented by the general formula [III]:

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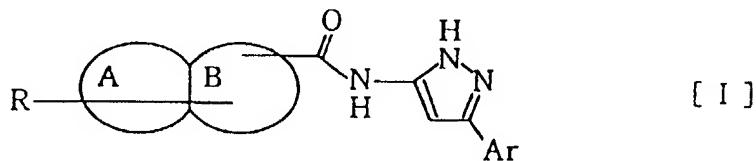


10 wherein A and B rings and R are as defined above,
or its reactive derivative.

12. A neuropeptide Y receptor antagonist comprising a compound represented by the general formula [I]:

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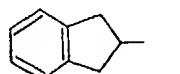
25 wherein A and B rings are ortho-condensed to each other, A ring represents an aromatic carbocyclic or heterocyclic ring and B ring represents an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed; Ar represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; and R represents a substituent selected from the group 30 consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, provided that when the group represented by

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is the group represented by

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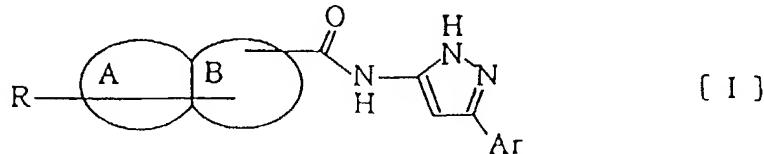


45 Ar is not a phenyl group nor a 4-chlorophenyl group,
or a salt thereof as an active ingredient.

13. An agent for the treatment of bulimia, obesity or diabetes comprising a compound represented by the general formula [I]:

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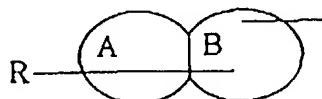
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EP 0 945 438 A1

wherein A and B rings are ortho-condensed to each other, A ring represents an aromatic carbocyclic or heterocyclic ring and B ring represents an aliphatic four- to seven-membered carbocyclic or nitrogen-containing heterocyclic ring, said nitrogen atom being possible to present at only the position where the A ring is condensed; Ar represents an aromatic carbocyclic or heterocyclic ring group which may have a substituent selected from the group consisting of a halogen atom and lower alkyl, lower alkenyl, lower haloalkyl, lower alkoxy, lower alkylthio, lower alkylamino, lower dialkylamino and aromatic carbocyclic ring groups; and R represents a substituent selected from the group consisting of a halogen atom and nitro, lower alkyl, lower alkoxy, aromatic carbocyclic ring groups and a carbonyl group having an aromatic carbocyclic ring group, or a hydrogen atom, provided that when the group represented by

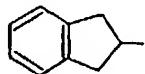
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is the group represented by

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Ar is not a phenyl group nor a 4-chlorophenyl group,
or a salt thereof as an active ingredient.

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INTERNATIONAL SEARCH REPORT		International application No. PCT/JP97/04567									
A. CLASSIFICATION OF SUBJECT MATTER Int. Cl ⁶ C07D231/40, 401/04, 403/04, 403/12, 405/12, 409/12, 487/04, A61K31/415, 31/47, 31/44 According to International Patent Classification (IPC) or to both national classification and IPC											
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) Int. Cl ⁶ C07D231/40, 401/04, 403/04, 403/12, 405/12, 409/12, 487/04, A61K31/415, 31/47, 31/44											
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched											
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CA (STN), REGISTRY (STN)											
C. DOCUMENTS CONSIDERED TO BE RELEVANT <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="text-align: left; padding: 2px;">Category*</th> <th style="text-align: left; padding: 2px;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="text-align: left; padding: 2px;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td style="padding: 2px;">A</td> <td style="padding: 2px;">JP, 62-175466, A (Beecham Group PLC.), August 1, 1987 (01. 08. 87) & GB, 8531019, A & EP, 227431, A</td> <td style="padding: 2px;">1 - 13</td> </tr> <tr> <td style="padding: 2px;">A</td> <td style="padding: 2px;">JP, 7-188269, A (Otsuka Pharmaceutical Factory, Inc.), July 25, 1995 (25. 07. 95) (Family: none)</td> <td style="padding: 2px;">1 - 13</td> </tr> </tbody> </table>			Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	A	JP, 62-175466, A (Beecham Group PLC.), August 1, 1987 (01. 08. 87) & GB, 8531019, A & EP, 227431, A	1 - 13	A	JP, 7-188269, A (Otsuka Pharmaceutical Factory, Inc.), July 25, 1995 (25. 07. 95) (Family: none)	1 - 13
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<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.											
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed											
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family											
Date of the actual completion of the international search February 12, 1998 (12. 02. 98)	Date of mailing of the international search report February 24, 1998 (24. 02. 98)										
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.										

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